UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,687	09/28/2000	David Wallach	WALLACH=25	7238

1444 7590 12/04/2002

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/04/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/671,687	WALLACH ET AL.	
	Examiner	Art Unit	
	David A Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *5-19 and 25-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/646,403* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that Group V is considered to be *prima facie* obvious over Group I. Applicant has presented an admission that the production of antibodies to the protein claimed in Group I would be *prima facie* obvious if the protein were known, and states the decision of *In re Gold*, 42 USPQ2d 1095 (Comm'r Pats 1996). In light of the decision, applicant invokes MPEP § 803.01, requesting that the inventions of Group I and Group V be examined together in the instant application. Applicant's arguments are found convincing, and applicant is hereby held to their admission that the antibodies are obvious in light of the protein claimed in Group I.

Claims 5-19 and 25-37 were cancelled by the applicant in the response to the Election/Restriction requirement, filed September 23, 2002 (Paper No. 10). Claims 1-4 and 20-24 are ready for examination in the instant application.

Priority

Concerning claims 2-4:

Applicant's claim for domestic priority to Application No. 09/646,403 under 35 U.S.C. 120 is acknowledged. However, the CIP application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 2-4 of this application. Claims 2-4 of the instant application are drawn to an isolated NAP protein, identified as SEQ ID NO: 3, and variants or fragments thereof. The priority application does not contain SEQ ID NO: 3 in the

sequence listing. As such, priority for claims 2-4 is given only for the filing date of the instant application, September 28, 2000.

Acknowledgment is made of applicant's claim for foreign priority based on two applications filed in Israel on September 1, 1998 (126024) and February 17, 2000 (134604). In view of the priority claim under 35 U.S.C. 120, claims 2-4 can only be granted priority to the 134604 application because the 126024 application is more than one year prior to the priority date concerning these claims. However, this application fails to provide adequate support under 35 U.S.C. 112 for claims 2-4 of this application for the same reasons as detailed above, therefore the priority date given for claims 2-4 is the filing date of the instant application, September 28, 2000.

Concerning claims 1 and 20-24:

Applicant's claim for domestic priority to Application No. 09/646,403 under 35 U.S.C. 120 is acknowledged. Applicant's claim for priority to international application PCT/IL99/00158 under 35 U.S.C. 365 is acknowledged. Acknowledgment is made of applicant's claim for foreign priority based on two applications filed in Israel on September 1, 1998 (126024) and February 17, 2000 (134604).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 24, 2001 (Paper No. 5) has been considered by the examiner, and a copy has been attached to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims any isolated protein that is capable of binding to NF-κB regulatory complex and TRAF2, wherein the protein is (a) not an antibody, (b) is present in a pharmaceutical preparation, or (c) is an antibody or the binding portion thereof. The claims read on a broad genus of proteins, pharmaceuticals containing the proteins, and antibodies directed towards the proteins.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims the proteins, pharmaceutical compositions and antibodies by function only (i.e., their ability to bind to TRAF2 and the NF-κB regulatory complex), without any disclosed or known correlation between the elements and their function. The claims read on any protein that can bind to TRAF2 and the NF-κB regulatory complex, but the specification only describes one specific embodiment, NAP (as represented by SEQ ID NO: 3). Furthermore, the specification does not provide a structural analysis of NAP to identify the relevant structural features that are required for binding activity. For example, is there a specific domain that can be found in multiple proteins that would allow the skilled artisan to envision the proteins that are claimed? Are there multiple proteins that are structurally divergent that can bind to TRAF2 and the NF-κB regulatory complex? The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification only discloses a single protein, rather than a representative number of species within the genus as claimed, and the specification does not indicate the relevant structural features that are required for the interaction to take place.

The prior art does not provide sufficient information on the subject to overcome the written description requirements. There is no description in the prior art that allows one to envision a representative number of proteins that bind to TRAF2 and the NF-κB regulatory complex. There is no description of the relevant structural features that are required for an interaction between TRAF2 and the NF-κB regulatory complex. There is no identification of a domain that has the capacity to bind to TRAF2 and the NF-κB regulatory complex. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship between a representative number of proteins that can bind to TRAF2 and the NF-κB regulatory complex nor the relevant structural features that are required for the interaction. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims "The isolated protein...variant/fragment having an amino acid sequence that is at least 85% identical with SEQ ID NO: 3...capable of binding to TRAF2 and the NF-κB regulatory complex. The claims read on a broad genus of protein variants.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not

disclose relevant identifying functional characteristics of the variant/fragment with respect to its ability to bind to TRAF2 and the NF-κB regulatory complex.

Applicant claims the protein variants by function only, without any disclosed or known correlation between the elements and their function. The claims read on any variant/fragment that is capable of binding to TRAF2 and the NF-κB regulatory complex. What are the relevant structural features of the protein represented by SEQ ID NO: 3 so that the skilled artisan knows what fragments can be used to interact with TRAF2 and the NF-κB regulatory complex? What 15% of the molecule can be altered without changing the functional characteristic of binding to TRAF2 and the NF-κB regulatory complex? The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification only discloses teachings regarding SEQ ID NO: 3 and its interaction with TRAF2 and the NF-κB regulatory complex.

The prior art does not provide sufficient information on the subject to overcome the written description requirements. There is no description in the prior art that allows one to envision a representative number fragments or variants of SEQ ID NO: 3 that retain a functional capacity to bind to TRAF2 and the NF-κB regulatory complex. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a representative number of deletions, additions or substitutions can be made in SEQ ID NO: 3 without changing its capacity to bind to TRAF2 and the NF-κB regulatory complex. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or

the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 20 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification does not provide an enabled use for pharmaceutical compositions as claimed.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of the invention. The nature of the invention is a pharmaceutical composition comprising a polypeptide that can bind to TRAF2 and the NF-κB regulatory complex or a pharmaceutical composition comprising an antibody that binds to the protein. The only apparent real world use for the compositions appears to be the treatment of individuals with a pathological disorder associated with NF-κB. NF-κB is involved in a vast number of biological processes and pathological disorders (see Baldwin *The Journal of Clinical Investigation* **107**: 3-6 (2001) for review; see entire document, especially Table 1), the regulation of its activity exists at a very

complex level and there are a number of aspects of NF-κB regulation that remain unknown in the art (see Ghosh *et al. Cell* **109**: S81-S96 (2002) for review; see entire document). A pharmaceutical composition comprising one protein involved in the regulation of NF-κB that can treat any pathological condition associated with NF-κB (i.e., the Nature of the invention) is a very complex invention. It is unclear how a single protein in a pharmaceutical composition can effectively treat *any* such condition, especially in light of the specification and the current state of the prior art. Furthermore, there is no specific affect as disclosed in the specification for the use of the pharmaceutical composition, only a generalized statement that it can be used to treat pathological conditions associated with NF-κB. What *specific* affect is applicant hoping to accomplish with the use of the pharmaceutical compositions?

Scope of the invention. The scope of the invention is very broad. Applicant claims the use of a pharmaceutical composition that can treat any pathological condition associated with NF-κB. It is not clear that the pharmaceutical composition as claimed can ably prevent any pathological disorder associated with induction of NF-κB. This is further complicated when considering the State of the art and the Nature of the invention.

State of the art. The state of the art regarding the use of peptide therapy is highly under-developed in the prior art. It is even less developed concerning the specific instance of using pharmaceutical compositions comprising polypeptides that bind to TRAF2 and the NF-κB regulatory complex to reduce the activation of NF-κB. As stated in the Nature of the invention, NF-κB is a highly regulated protein involved in a complex number of responses and pathological disorders, and there are still many aspects of NF-κB regulation that are unclear. There are no specific examples of using pharmaceutical compositions comprising polypeptides that bind to

TRAF2 and the NF-κB regulatory complex to reduce the activation of NF-κB, thus the skilled artisan cannot turn to the prior art for guidance on how to use the invention. Therefore, the skilled artisan would be required to perform undue and unpredictable trial and error experimentation to use the invention in light of the prior art.

Number of working examples and Guidance provided by applicant. The specification provides no guidance or working examples on how to use the claimed invention, thus it cannot overcome the deficiencies of the State of the Art. The specification merely discloses how the polypeptide of the invention was identified and cloned, and suggests uses for the polypeptide in pharmaceutical compositions for the treatment of individuals with pathological disorders associated with induction of NF-κB. In the absence of guidance from the specification, the skilled artisan would be required to perform undue and unpredictable trial and error experimentation to use the invention as claimed.

Level of skill in the art. The level of skill in the art of peptide therapy, specifically with regard to using polypeptides that bind to TRAF2 and the NF-κB regulatory complex (which thereby regulates the activity of NF-κB), is under-developed. This is evidenced by a lack of effective examples in both the prior art and the instant specification for treating a disease using polypeptides that bind to TRAF2 and the NF-κB regulatory complex.

Unpredictability of the art. The art is highly unpredictable. This is evidenced by the absence of working examples and guidance in both the instant specification and the prior art on how to use a pharmaceutical composition to treat a pathological condition associated with NF-κB. The nature of the invention is very complicated, the level of skill in the art is underdeveloped, and the

skilled artisan is deprived of guidance in both the prior art and the instant specification to how to use the invention.

Amount of experimentation required. Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have conducted undue and unpredictable trial and error experimentation in order to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "NF-κB regulatory complex" in claim 1 is a relative term which renders the claim indefinite. The term "NF-κB regulatory complex" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. On page 30 of the instant specification, applicant defines the "NF-κB regulatory complex" as having 'main components'. It is unclear if these are the only components that are being considered in the binding of a protein to the regulatory complex, or if there are other components to which a protein can bind and still be considered as binding to the "NF-κB regulatory complex". Without knowing what is and is not included in the "NF-κB regulatory complex", it is impossible to know if a protein binds to it.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. The claim indicates an isolated protein that is capable of binding to NF-κB regulatory complex and TRAF2. Does the protein bind to the NF-κB regulatory complex and TRAF2 simultaneously? Can the protein bind with the NF-κB regulatory complex and TRAF2 in two separate complexes, or must it be the same complex?

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
November 27, 2002

PATENT EXAMINER
Art Unit 1636